UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,164	04/04/2005	Susanne Binder	34157-707.831	5602

21971 7590 06/06/2007

WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	
MAIL DATE	DELIVERY MODE
06/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,164	BINDER ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42, 43, 45-49 and 53-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42, 43, 45-49 and 53-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 42, 43, 45-49 and 53-61 are pending.

Election/Restrictions

Applicant's election of species (age-related macular degeneration and therapeutic drugs) in the reply filed on Apr. 3, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, the examiner has withdrawn the requirement of species election for Group B. All species listed in claim 49 have been examined.

It is noted that applicant has elected Group VII invention (claims 42-49) in the reply filed on Dec. 18, 2006.

Claims 44 and 50-52 are canceled and claims 53-61 are newly added. Claims 42, 43, 45-49 and 53-61 have been considered on the merits.

Claim Objections

Claim 60 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since the independent claim of the current claim contains species of growth factors, enzyme or therapeutic drugs, the species disclosed in claim 60 do not further limit "enzyme" of claim 49 because the species listed in claim 60 do not belong to enzyme.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 discloses the number of cells "about 16,000 to about 20,000 per 4 mm^2". It is not clear what the unit of the number of cells intends to point out. It could be 4 mm^2 of anything. Apparently the unit would be of the amniotic membrane, but the current claim does not particularly point out the subject matter. Clarification is required.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 47 recites the

broad recitation "cells cultured on the amniotic membrane", and the claim also recites "retinal pigment epithelial cells" which is the narrower statement of the range/limitation. The limitation of "cells cultured on the amniotic membrane" could be any cell including "retinal pigment epithelial cells", therefore, the limitation is also not further limiting of claim 42. For the search purpose, the limitation is interpreted as "retinal pigment epithelial cells being cultured on the amniotic membrane."

Claim 55 discloses a limitation to the method steps of claim 54 having additional step of adding mesenchymal cells to at least one side of the stroma. It is not clear where this additional step would be carried out in the method steps of claim 42 and 54. It could be added after the treating, during the treating or the mesenchymal cells added to the stroma before the treating using the method steps of claim 42.

Similarly, claim 57 discloses additional step to the method steps of claim 42. It is not clear whether the additional step of treating the amniotic membrane with excimer laser ablation is during, before, or after the treatment of claim 42.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 56 and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 56 discloses a limitation to the mesenchymal cells of claim 55 being fibroblast. However, there is no description in the specification of this limitation. In the specification, the mesenchymal cells are disclosed (see paragraph [0026]), however, it is not described that the mesenchymal cells of the claim being fibroblasts. Although fibroblasts are known to be mesenchymal cells, it is not clearly described in the specification. Therefore, the instant claim introduces a new matter situation to the current invention.

The limitation of "cells that have been immortalized by viral agents or non-viral agents" in claim 59 does not have proper support in the specification. There is a disclosure of "RPE cells that have been immortalized by viral agents or non-viral agents" in paragraph [0048], however, there is not disclosure for the broader limitation of the claim 59. Thus, this limitation introduces a new matter situation to the current invention.

Claim 59 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for retinal pigment epithelial cells that have been immortalized by viral agents or non-viral agents, does not reasonably provide enablement for ANY cell that has been immortalized by viral agents or non-viral agents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the

state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The limitation of "cells that have been immortalized by viral agents or non-viral agents" is so broad as to encompass ANY cells that have been immortalized by viral agents or non-viral agents. The scope of this claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of cells broadly encompassed by the claims. Since the current invention requires a specific type of cells such as retinal pigment epithelial cells, any other types of cells, no matter how they become immortalized, would not enable the current method steps for treating retinal disorders. For example, terminally differentiated and immortalized muscle cells, PC12 cells, or other tumor cell lines would not effectively treat a retinal disorder, no matter how they are immortalized.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 43, 45-46, 49, 54 and 57-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (US 6,045,791; IDS reference #7) in view of Dutt et al. (1991; IDS ref. #15).

Claims 42, 43, 45-46, 49, 54 and 57-61 are drawn to a method for treating a retinal disease, comprising inserting a composite comprising amniotic membrane and retinal pigment epithelial cells in a subretinal space of a patient in need thereof (claim 42); a limitation to the epithelial cells being from about 16,000 to about 20,000 per 4 mm^2 of the amniotic membrane (claim 43); a limitation to the retinal disease being age-related macular degeneration (claim 45); a limitation to the amniotic membrane being human (claim 46); a limitation to the retinal pigment epithelial cells being cultured on the amniotic membrane (claim 47); a limitation to the amniotic membrane comprising a basement membrane and a stroma (claim 54); a limitation to the amniotic membrane being treated on one side with excimer laser ablation (claim 57); a limitation to the excimer laser ablation altering the thickness of the stromal side or basement membrane of the amniotic membrane (claim 58); a limitation to the retinal pigment epithelial equivalent cells being iris pigment epithelial cells, retinal pigment epithelial cells differentiated from an adult or embryonic stem cell, cells derived from neural retinal cells

or cell derived from a ciliary body (claim 59); a limitation to the pharmaceutically active molecule being retinal pigment epithelium-derived growth factor, transforming growth factor-beta or interleukin-10 (claim 60); a limitation to the composite being formed by applying retinal pigment epithelial cell or its equivalent to an amniotic membrane, and culturing the cells on the membrane under the condition for growth (claim 61).

Liu teaches a method of treating a retinal disorder such as age-related macular degeneration, by transplanting retinal pigment epithelium (RPE) cells cultured on an attachment substrate into the subretinal area of a patient in need thereof (see Abstract and column 7, lines 57-59 and 65-67; Example 1).

Liu does not teach the use of amniotic membrane.

Dutt et al. teach the use of human amniotic membrane as a substrate for culturing retinal pigment epithelial cells (see whole document).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to replace the collagen substrate of Liu with the amniotic membrane of Dutt et al. in the method of Liu.

The skilled artisan would have been motivated to make such a modification because both the substrate of Liu and the amniotic membrane of Dutt et al. are used for the growing RPE cells, they are considered as art-recognized equivalents for growing RPE cells for transplantation.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core

of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

Although Liu in view of Dutt et al. do not particularly teach the number of cells on the amniotic membrane, however, because the number of cells used in the claimed method is considered as one of result effective variables. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C

and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed atl a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the :references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling; 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Although Liu in view of Dutt et al. do not particularly disclose the presence of "pharmaceutically active molecule" in the method, since it is well known in the art that the amniotic membrane contains various growth factors, the limitation of "pharmaceutically active molecule" is inherently accomplished by the use of amniotic membrane. Since Dutt et al. disclose a culture condition of human pigment epithelial cells on the amniotic membrane using culture medium containing growth factors, enzymes and therapeutic drugs, the method of Liu in view of Dutt et al. would contain a

composite comprising amniotic membrane and RPE cells with other growth factors, enzymes and/or therapeutic drugs because of culturing condition of the RPE cells.

Although Liu in view of Dutt et al. do not particularly teach the use of excimer laser ablation technique, since it is necessary to cut the substrate, having RPE cells grown on it, for transplantation as described in Liu (see Example 1, column 11, lines 10-11), and excimer laser ablation technique is well known in the art to cut and reshape variety of tissues, it would have been obvious for a person of ordinary skill in the art to optimize the cutting procedure by using a technique with high precision such as excimer laser ablation technique. Further, a surgical instrument used in the method of Liu for cutting the substrate containing RPE cells and excimer laser ablation would be considered as art-recognized equivalents, and therefore, the excimer laser ablation would be used in place of the surgical instrument for cutting the substrate for transplantation.

The limitation of claim 58 is considered as a result of the method step in claim 57. Claim 58 contains a "wherein" clause that merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.*, 57 USPQ2d 1747 (Fed. Cir. 2001).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Dua et al. (1999; IDS ref. #19).

Claims 48 and 49 are drawn to a limitation to the composite further comprising a pharmaceutically active molecule (claim 48); a limitation to the pharmaceutically active molecule being growth factors, enzymes, or therapeutic drugs (claim 49).

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Although Liu in view of Dutt et al. do not teach the presence of "pharmaceutically active molecule" in the composite of the method, the limitation of "pharmaceutically active molecule" is inherently accomplished by the use of amniotic membrane of Dutt et al. in the method of Liu. Because Dua et al. teach the amniotic membrane produces various growth factors such fibroblast growth factor (see p.748, right column, a section under the title of "Amniotic membrane in ophthalmology").

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Grueterich et al. (2002; IDS ref. #28).

Claim 53 is drawn to a limitation to the amniotic membrane being epithelially denuded.

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. do not teach the amniotic membrane being epithelially denuded.

Grueterich et al. teach the use of epithelially denuded amniotic membrane in culturing limbal epithelium (see whole document; p.64, Materials and Method).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use epithelially denuded amniotic membrane of Grueterich et al. in the method of Liu in view of Dutt et al.

The skilled artisan would have been motivated to make such a modification because both intact and epithelially denuded amniotic membrane would be suitable for support of epithelial cell culture. Since amniotic membrane is a suitable substrate for culturing not only corneal epithelial cells as taught by Grueterich et al. but also for RPE cells, a person of ordinary skill in the art would have considered the choice of intact or denuded amniotic membrane as a routine optimization procedure to obtain optimal environment for culturing RPE cells for treating a retinal disorder.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Claims 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu (supra) in view of Dutt et al. (supra), in further view of Tseng (US 6,152,142; IDS ref. #1).

Claims 55 and 56 are drawn to a limitation to the method further comprising a step of adding mesenchymal cells to one side of the stroma (claim 55); a limitation to the mesenchymal cells being fibroblasts (claim 56);

Liu in view of Dutt et al. render the subject matter of claim 42 obvious (see above).

Liu in view of Dutt et al. do not teach a step of adding mesenchymal cells to the stroma of the amniotic membrane or the mesenchymal cells being fibroblasts.

Tseng teaches that when fibroblasts (mesenchymal cells) are grown in the stromal side of amniotic membrane, it provides an environment comparable to isolated collagen (fibroblasts are collagen-producing cells) and better cell growth in culture than a plain plastic surface.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to add fibroblasts on the stromal side of the amniotic membrane of Liu in view of Dutt et al.

The skilled artisan would have been motivated to make such a modification because Tseng teaches an advantage given by the fibroblast culture on the stromal side of the amniotic membrane providing better cell culture environment for epithelial cells.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taeyoon Kim
Patent Examiner
Art Unit 1651

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651